Maintaining health in old age through homeostasis

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The central hypothesis of Switchbox is that control of homeostasis by the hypothalamus will be better preserved in the offspring of long-lived sibling who age in better health compared to their partners that show *regular* ageing. This, we...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON35448

Source
ToetsingOnline

Brief title
Switchbox

Condition

- Other condition

Synonym
healthy ageing, longevity

Health condition

betreft gezonde proefpersonen zonder aandoening

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: Ageing, Homeostasis, Hypothalamic output

Outcome measures

Primary outcome

Offspring/Partner Neuro-endocrine output characterization via:

24 hours hormone rhythm measurement (ACTH, TSH, fT4, fT3, cortisol, insulin,

glucose, adiponectin)

Offspring/Partner Peripheral metabolism characterization via:

Glucose sampling using continuous glucose monitor

Indirect calorimetry using ventilated hood

Core body temperature

Diet and activity monitoring using diaries and accelerometry

Physical activity measurement using tri-axial accelerometer

Characterization of Brain functions in Offspring/Partners, via:

* Functional MRI studies in stressed and non-stressed condition

o Reaction times on the Working Memory (WM) task

- Offspring (Stress > no stress) < control (Stress > no stress)

- Brain activation during emotional WM task performance: (associated with

impaired task performance)

o Amygdala functional connectivity:

- Controls (Stress > no stress) > Offspring (Stress > no stress)

o Dorsolateral Prefrontal Cortex: Stress < no stress; Ventral PFC, lateral PFC

and amygdala: Stress > no stress

We expect offspring to show smaller stress effects on the reciprocal relation

between dorsal and ventral brain activation compared to controls.

* Cognition and mood (test batteries)

* Sleep (via diaries and accelorometry)

Secondary outcome

na

Study description

Background summary

Although life expectancy is increasing, very few people achieve healthy longevity, making the identification of biological and homeostatic mechanisms that regulate the rate of ageing, and therewith contribute to the onset or prevention of age-related disease, of extreme importance. All aspects of mental and physical health are critically dependent upon appropriate reception, processing and integration of internal and external signals and the capacity to mount adaptive responses. This critical Homeostatic (the ability to dynamically adapt to environmental challenge whilst maintaining the composition of the *milieu intérieur* within certain limits) role is played by the hypothalamus. Thus, an understanding of the hypothalamic control of homeostasis is a key to understanding the mechanisms that drive healthy ageing.

Switchbox will study the diffrences in hypothalamic control of homeostasis in offspring of long-lived sibling of Leiden Longevity study, who have been shown to age in better health compared to their partners who show *regular* aging.

Study objective

The central hypothesis of Switchbox is that control of homeostasis by the hypothalamus will be better preserved in the offspring of long-lived sibling who age in better health compared to their partners that show *regular* ageing. This, we hypothesize, will be reflected in differences in brain function, neuro-endocrine output and peripheral metabolism. To achieve the central objective, the study will be conducted in three phases (see Protocol ID P11.116, pages 12 &13). Below are the objectives specific for phase I.

Phase I objectives:
1. To compare brain function in offspring of long-lived siblings (cases) and their partners (controls) via brain fMRI measurements; cognition and mood as well as assessment of sleep and feeding patterns.

2. To compare neuro-endocrine output and rhythms (hypothalamo-pituitary-adrenal axis, hypothalamo-pituitary-thyroid axis and insulin-IGF- signalling pathway) of offspring of long-lived siblings (cases) and their partners (controls) over a 24h period.
3. To compare peripheral metabolism in offspring of long-lived siblings (cases) and their partners (controls) by assessing glucose metabolism, oxygen consumption, CO2 production and Physical activity.

Study design

Phase 1 of Switchbox is a single-blind case-control observational study. We will include 60 couples, consisting of an offspring of long-lived siblings (case) and his/her current partner (control). The couples shall be divided into 2 groups: A and B.

For subjects in group A (20 couples), we will measure brain function (BF,), neuro-endocrine output (NEo), and peripheral metabolism (PM) over 10 study days In group B (40 couples), we will measure brain function and peripheral metabolism over 8 study days. The study will be carried out at the research center of Leiden University Medical Center (LUMC). {See protocol ID11.116, pages 13-16}

Study burden and risks

The total study will be carried out in 60 couples, which will be divided into two groups (groups A and B).
Group A (20 couples) will undergo the full spectrum of tests to elicit the main study parameters in10 days, encompassing two and half intensive study days (2 nights at the hotel and 24 hour admittance to the hospital).
* Day 1 (morning only): fMRI (resting state, after stress (TSST) using 3T), measurement of cognition and insertion of a continuous glucose monitor (CGM).
* Day 2: 24 hour hormone sampling (maximum of 432 ml blood over 24 hours in 10 minutes intervals).

* Day 3 (morning only): Indirect calorimery using a ventilated hood (fasted and after ingestion of glucose).
The ensuing 7 days (non- intensive phase) involve keeping a simple 7-day sleep, food and activity diary, accelerometry, and removal and return (by post) of the CGM on study day 5.
Group B (40 couples) will undergo a selection of tests in 8 days, encompassing fMRI testing, CGM, accelerometry and diaries, but not 24 hour hormone sampling or calorimetry. They will come to the study centre once (day 1), without having to stay overnight.
* Day 1: fMRI (resting state, after stress (Triers social stress test) using 3T), measurement of cognition and insertion of a continuous glucose monitor (CGM).
The ensuing 7 days (non- intensive phase) involve keeping a simple 7-day sleep, food and activity diary, accelerometry, and removal and return (by post) of the CGM on study day 5.
The fMRI, CGM, accelerometry and indirect calorimetry are procedures that are minimally invasive. 24-hour blood sampling, though invasive, does not exceed the amount of blood drawn during blood transfusion. There are no direct benefits to the subjects, and so subjects will be financially compensated for their time and burden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Couples from the Leiden Longevity Studie, consisting of a child from a longlived family (case) and his/her current partner (control)

Exclusion criteria

Endocrin problems: diabetes, thyroid and adrenal problems
MRI: metal (parts) in the body and claustrofobia

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-05-2012
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	19-10-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-01-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-05-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL37635.058.11